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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/705,447	11/10/2003	Xiao Xu	ACE-00101.P.1.1-US	4588

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EXAMINER	
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ART UNIT	PAPER NUMBER
1797	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/705,447	XU ET AL.	
	Examiner	Art Unit	
	NATHAN A. BOWERS	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-13,15-26,29-32,34-44,47-50,72 and 287-310* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-13,15-26,29-32,34-44,47-50,72 and 287-310* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *121707*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 17 December 2007 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1) Claims 1-3, 7-13, 15, 25, 26, 36, 38-40, 43, 72, 287, 288, 290-297, 309 and 310 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolf (US 6280586) in view of Gerwen (US 6440662).

With respect to claims 1, 8, 9, 36, 43, 72, 287, 288, 290-293, 309 and 310, Wolf discloses a device for detecting cells comprising a non-conductive substrate (Figure 2:5) having two opposing ends, and a plurality of electrode arrays positioned on the substrate. Each electrode array comprises at least two electrodes (Figure 2:10), and electrically conductive trances and connection pads are in communication with the electrode arrays. The electrodes are used to detect impedance changes resulting from attachment of cells to the electrode surface. This is described in column 2, lines 39-55, column 3, lines 11-28, and column 7, lines 29-50. Column 7, line 63 to column 8, line 12 indicates that the electrodes have a surface (Figure 5:13) that is suitable for cell attachment and growth. Wolf, however, does not expressly state that the electrodes in each array have a width of more than 1.5 to 15 times the width of the gap between the electrodes.

Gerwen discloses an impedimetric detection system that comprises a plurality of interdigitated electrodes. Detection of an analyte is determined based on the interference of an electrical field between the electrodes. This is disclosed in column 3, line 40 to column 4, line

11 and in column 10, lines 40-52. It is clear from the Figure 1C that the width of the electrodes is between 1.5 and 15 times the width of the gap between the electrodes.

Wolf and Gerwen are analogous art because they are from the same field of endeavor regarding microelectronic cell sensor devices.

At the time of the invention, it would have been obvious to one of ordinary skill in the art to alter Wolf's device to ensure that the electrode widths were more than 1.5 and less than 15 times the non conductive material width if it was determined through trial and error that this configuration produced the best results. This limitation is considered to be a result effective variable that is optimized through routine experimentation. This position is supported by Gerwen, who indicates that electrode width and gap sizes all depend on several considerations that involve engineering tradeoffs. Gerwen states in column 3, lines 1-8 and column 4, lines 1-11 that a small gap to electrode width ratio results in a high degree of miniaturization and an increase in sensitivity.

With respect to claims 2 and 3, Wolf and Gerwen disclose the apparatus in claim 1 wherien the substrate comprises glass, sapphire or silicon. This is described by Wolf in column 7, lines 29-50.

With respect to claims 5, 7, 10, 11 and 13-15, Wolf and Gerwen disclose the apparatus in claim 1 wherein up to half of the electrical traces extend to one end of the substrate, and the remaining electrical traces extend to the other end of the substrate. The electrodes are of equal width and are evenly spaced. Figure 2 of Wolf indicates that the electrodes are organized in an

interdigitated fashion, and that a bus is associated with the plurality of electrodes in each electrode array. It is apparent from the Figures that a gap on the substrate exists between the bus and the array of electrodes, thus forming an area of non conductive material.

With respect to claim 12, Wolf and Gerwen disclose the apparatus in claim 10 wherein each array of electrodes is organized in a sinusoidal fashion. This is disclosed by Wolf in Figure 1. Additional electrodes designs, such as concentric, castellated, and honeycomb, are considered to be obvious variants from the sinusoidal and comb designs disclosed by Wolf. These other designs would not perform differently than the designs set forth in the prior art, and therefore do not constitute a patentable difference. See MPEP 2144.04.

With respect to claims 25, 26 and 40, Wolf and Gerwen disclose the apparatus in claim 1. Furthermore, both Wolf and Facer disclose the use of impedance analyzers electrically connected to the array electrodes through conductive traces. Specifically, this is described by Wolf in column 3, lines 37-49.

With respect to claims 38 and 39, Wolf and Gerwen disclose the apparatus in claim 1. Wolf additionally discloses a method for using the apparatus. Impedance measurements are generated when target cells are positioned directly on the electrodes as well as when the target cells are suspended in fluid around in the electrodes in order to determine to what degree cell adhesion affects communication between the reference and measuring electrodes. Cells are supplied with a culture media sufficient for target cell growth.

With respect to claims 294 and 296, Wolf and Gerwen disclose the apparatus in claim 1. Although not expressly disclosed by the references, electrode structures comprising indium tin oxide, chromium, gold, copper, nickel, platinum, silver, titanium, steel and aluminum are considered to be well known in the art. Optically transparent electrodes are considered to be well known in the art.

With respect to claims 296 and 297, Wolf and Gerwen disclose the apparatus in claim 1 wherein the surfaces of the electrodes are modified with a cell-adhesion promotion moiety. Column 7, line 63 to column 8, line 12 states that an interlayer (13) is provided to encourage cell growth on the electrode surfaces. Gerwen additionally states in column 3, lines 45-63 that biochemical probes are assembled on the surfaces of the electrodes to facilitate binding.

2) Claims 4, 16-24, 29-32, 34, 44, 47-50, 289 and 298-308 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolf (US 6280586) in view of Gerwen (US 6440662) as applied to claims 13 and 15, and further in view of Wolf (US 6376233).

With respect to claims 4, 16-24, 29-32, 34, 44, 47-50 and 289, Wolf '586 and Gerwen disclose the apparatus set forth in claims 13 and 15 as set forth in the 35 U.S.C. 103 rejection above, however do not expressly indicate that a plurality of receptacles are disposed on the nonconductive substrate to produce fluid tight containers.

Wolf '233 discloses an apparatus and method for recording electrophysiological activity of biological cells. A plurality of sensors (Figure 4:7) are provided to correspond with the wells (Figure 3:10) formed by a microtiter plate (Figure 3:11). This is described in column 6, lines 17-

30 and in Figures 3-6. Each sensor array (Figure 4:7a) includes at least one stimulus electrode capable of interacting with cells. Wolf additionally discloses a retaining part (Figure 3) capable of culturing cells in a region directly above the sensor array.

Wolf '586, Gerwen and Wolf '233 are analogous art because they are from the same field of endeavor regarding microfluidic devices that are used to electrically monitor cells.

At the time of the invention, it would have been obvious to provide the device proposed by Wolf '586 and Gerwen with a solution retaining part capable of culturing cells. This would have been beneficial because it would have allowed one to encourage cell growth at the integrated electrode, thus removing the need to transport the cell sample from a remote location to the sensor. By eliminating this transportation step, one would be able to increase efficiency and reduce contamination and fluid loss.

With respect to claims 298-308, Wolf '586, Gerwen and Wolf '233 disclose the apparatus set forth in claim 16 as set forth in the 35 U.S.C. 103 rejection above. The Wolf references additionally disclose a method for using the apparatus. Impedance measurements are generated when target cells are positioned directly on the electrodes as well as when the target cells are suspended in fluid around in the electrodes in order to determine to what degree cell adhesion affects communication between the reference and measuring electrodes. Cells are supplied with a culture media sufficient for target cell growth. Resistance ratios are determined by dividing a measured resistance when cells are attached to the electrode structure by a baseline resistance, and cell attachment and/or growth is monitored on a real time basis.

3) Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wolf (US 6280586) in view of Gerwen (US 6440662) as applied to claim 1, and further in view of Surridge (US 20030116447).

Wolf and Gerwen disclose the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above. Additionally, Wolf discloses that the device is produced by providing a non-conductive substrate. Wolf, however, does not state that a conductive film is deposited on the substrate, or that electrodes are patterned using laser ablation of the conductive film.

Surridge discloses a substrate that includes a plurality of electrode arrays capable of detecting an analyte in a sample solution. Paragraphs [0079]-[0082] indicate that interdigitated electrode arrays (Figure 1) are formed from a conductive film using laser ablation.

Wolf, Gerwen and Surridge are analogous art because they are from the same field of endeavor regarding biological detection systems.

At the time of the invention, it would have been obvious to create the electrodes disclosed by Wolf using a conductive film modified by a laser ablation process. Surridge states that laser ablation techniques are well known in the art, and that suitable lasers are widespread and commercially available. Surridge suggests that laser ablation techniques employing the use of a conductive film are especially suited for the creation of interdigitated microelectrodes.

4) Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wolf (US 6280586) in view of Gerwen (US 6440662) as applied to claim 1, and further in view of Gomez (US 20030157587).

Wolf and Gerwen disclose the apparatus set forth in claim 1 as set forth in the 35 U.S.C.

103 rejection above, however do not expressly state that capture reagents are immobilized on the surfaces of the electrodes.

Gomez discloses a microelectronic cell sensor that comprises a substrate (Figure 14:54) and a plurality of electrodes (Figure 14:36) capable of determining the presence of cells in a sample solution. Paragraphs [0087] and [0112] state that antibodies (Figure 14:76) are attached to the electrodes and the substrate in order to selectively bind to target bacteria cells (Figure 14:78). A difference in electrical measurements between the electrodes and a reference electrode indicates the presence of target cells in the detection chamber. The binding antibodies disclosed by Gomez are considered to be capable of being isolated from an extracellular matrix, and capable of binding to a cell surface receptor.

Wolf, Gerwen and Gomez are analogous art because they are from the same field of endeavor regarding microelectronic cell sensor devices.

At the time of the invention, it would have been obvious to attach antibodies and other biological molecules to the substrate disclosed by Wolf and Gerwen. This would have provided an established binding area suitable for cell attachment, and would have allowed one the ability to dictate the location of cells during detection. Gomez teaches in paragraph [0032] that the use of biological binding molecules are beneficial because they can be used to purify a cell sample prior to detection, thereby ensuring that any recording changes in impedance is due solely to the presence of cells rather than contaminants in the solution.

5) Claims 41 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolf (US 6280586) in view of Gerwen (US 6440662) as applied to claim 40, and further in view of

Sugihara (US 6132683).

Wolf and Gerwen disclose the apparatus set forth in claim 40 as set forth in the 35 U.S.C. 103 rejection above, however do not expressly state that a mechanical clip is provided for securely engaging the substrate in electrical contact with a trace.

Sugihara discloses a microelectronic cell sensor array comprising a substrate (Figure 2:2) covered by a non conductive film. As best seen in Figures 3 and 4, four electrode arrays are positioned on the substrate so that each array includes a plurality of electrodes connected to conductive patterns (Figure 4:12) and contacts (Figure 4:7). Each array additionally comprises a reference electrode (Figure 4:10). This is disclosed in column 6, lines 32-67. Column 2, lines 35-67 indicate that the cell activity is determined by measuring changes in impedance recorded by the electrodes. Column 6, lines 20-31 states that the substrate (Figure 2:2) is engaged by a holders (Figure 2:3,4) that function as a mechanical clip. The holders are adapted to form an electrical connection with the traces on the substrate and with a printed circuit board (Figure 2:5).

Wolf, Gerwen and Sugihara are analogous art because they are from the same field of endeavor regarding microelectronic cell sensor devices.

At the time of the invention, it would have been obvious to provide the apparatus of Wolf with a mechanical clip capable of securely engaging the substrate in electrical contact with a trace. As evidenced by Sugihara, this structural relationship is known in the art. The use of a mechanical clip provides an inexpensive and simple way to ensure that the substrate is reliably in electrical communication with a trace.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the `"right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6) Claims 1, 4, 25, 38-40 and 72 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2 and 58 of copending Application No. 11055639 in view of Gerwen (US 6440662).

The claims of Application No. 11055639 disclose a device and method for detecting cells that comprises a non-conductive substrate and a plurality of electrode arrays wherein each electrode array comprises at lest two or more electrodes. Electrically conductive traces and connection pads are provided. The claims of Application No. 11055639, however, do not state that specifics regarding electrode width and positioning.

Gerwen discloses the device as previously described above.

At the time of the invention, it would have been obvious to one of ordinary skill in the art to alter the device of Application No. 11055639 to ensure that the electrode widths were more

than 1.5 and less than 10 times the non conductive material width if it was determined through trial and error that this configuration produced the best results. This limitation is considered to be a result effective variable that is optimized through routine experimentation. This position is supported by Gerwen, who indicates that electrode width and gap sizes all depend on several considerations that involve engineering tradeoffs. Gerwen implies that it is known in the art to consider a variety of width sizes in order to produce the best configuration for the current experiment.

This is a provisional obviousness-type double patenting rejection.

7) Claims 1, 4, 25, 38-40 and 72 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 51, 72 and 75 of copending Application No. 10987732 in view of Gerwen (US 6440662).

The claims of Application No. 10987732 disclose a device and method for detecting cells that comprises a non-conductive substrate and a plurality of electrode arrays wherein each electrode array comprises at lest two or more electrodes. The use of an impedance analyzer is additionally described. Conductive traces and bonding pads are considered to be well known in the art. The claims of Application No. 10987732, however, do not state that specifics regarding electrode width and positioning.

Gerwen discloses the device as previously described above.

At the time of the invention, it would have been obvious to one of ordinary skill in the art to alter the device of Application No. 10987732 to ensure that the electrode widths were more than 1.5 and less than 10 times the non conductive material width if it was determined through

trial and error that this configuration produced the best results. This limitation is considered to be a result effective variable that is optimized through routine experimentation. This position is supported by Gerwen, who indicates that electrode width and gap sizes all depend on several considerations that involve engineering tradeoffs. Gerwen implies that it is known in the art to consider a variety of width sizes in order to produce the best configuration for the current experiment.

This is a provisional obviousness-type double patenting rejection.

Response to Arguments

Applicant's arguments with respect to the 35 U.S.C. 103 rejections involving the combination of Wolf with Caillat have been fully considered and are persuasive. Therefore, these rejections have been withdrawn. However, upon further consideration, a new ground of rejection is made in view of the combination of Wolf with Gerwen.

The Gerwen clearly discloses that it is known in the art to construct electrode arrays in such a way that width of the electrode elements is between 1.5 and 15 times the width of the gap between electrode elements. The Gerwen reference is unlike the previously applied Caillat reference because it is designed to measure impedance changes resulting from the attachment of a biological analyte to the surface of an electrode array (whereas Caillat is drawn to the fixation of reagents to reception electrodes). Although Gerwen teaches that the apparatus is specifically designed to measure the presence of a specific enzyme and/or nucleic acid, one of ordinary skill in the art would understand that Gerwen's apparatus could be used to monitor cell binding

according to the same basic principles. Just as the binding of biochemical compounds affects the conductivity between electrodes, so would the binding of a cell. Accordingly, Gerwen and Wolf are analogous art, and one of ordinary skill in the art would know to look to the teachings of Gerwen regarding electrode configuration when optimizing the apparatus of Wolf.

Conclusion

This is a non-final rejection.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan A. Bowers whose telephone number is (571) 272-8613. The examiner can normally be reached on Monday-Friday 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys Corcoran can be reached on (571) 272-1214. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

//William H. Beisner//
Primary Examiner, Art Unit 1797

/Nathan A Bowers/
Examiner, Art Unit 1797